A SUMMARY OF COST-EFFECTIVENESS CALCULATIONS IN THE DIAGNOSIS AND TREATMENT OF HYPERTENSIVE RENOVASCULAR DISEASE*

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IN a thought-provoking article titled "Radiology — A Case Study in Technology and Manpower" in *The New England Journal of Medicine* several years ago, John Knowles made the following statement: "One could and should ask how many renal arteriograms in patients with hypertension have resulted directly in the surgical or medical cure of the patient's hypertension.... Increasingly we shall be asked to answer such a question, for our resources are not infinite nor is our share of the Gross National Product."[1]

This statement focuses on one of the central problems in medicine today: How can we measure the impact of the diagnostic modalities which we are using in medical management? This impact can be measured in three ways. First, we can determine how many patients with a given disease we can locate with our detection program. Second, we can determine the probability that a patient has the disease given the results of one or more diagnostic examinations. Third, we can estimate the gain to the individual and society from identifying patients with disease.

All of these measures are associated with costs—a financial cost and a "life cost." The financial cost, obviously, is the cost in dollars of the diagnostic work-ups of all patients afflicted with or thought to be afflicted with the disease in question. In practice, this financial cost should be realistic in terms of the total financial allotment for medical care. The meaning of the "life cost" is not so simple. In its fundamental aspects it

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involves the lives lost in and the morbidity associated with the diagnostic work-up—not only the lives of those patients with disease but also of those who are incorrectly thought to have disease. This "life cost" should not be greater than the potential number of lives gained by the identification and treatment of those with the disease. How much less it should be is not clear.

The problem of hypertension was selected for this case study to exemplify some techniques which can be employed in measuring the utility of various diagnostic modalities. The use of the intravenous pyelogram (IVP) and the renogram (RG) was studied in isolating patients with renovascular disease from those with other forms of hypertension; the sensitivity of these examinations was investigated singly and in combination in order to determine the expected yields in a representative hypertensive population. In addition, preliminary calculations of the costs of screening the hypertensive population in the United States by these radiographic modalities were made.

Data collected by the Cooperative Study of Renovascular Disease were used for this investigation. We analyzed scintigraphic and radiographic data on more than 1,000 patients, all of whom had renal angiography; 771 of these patients had no identifiable cause of their hypertension ("essential hypertension") and 288 had renal artery disease demonstrated angiographically.

Iodohippuran renograms (RGs) were analyzed according to the method of Burrows and Farmelant.[2,3] The degree of functional asymmetry between the two kidneys is graded from 0 to 1, where symmetrical function is associated with a value near 1 and asymmetric function with varying grades less than 1.

Most hypertensive patients who do not have renovascular disease (RVD–) have symmetrical function, that is, values between 0.9 and 1.0, whereas patients who have renovascular disease (RVD+) show a much greater range of symmetry in renal function. When the data from the RG are plotted in the form of a receiver operating characteristic (ROC) curve, that is, a plot of the true positive (TP) ratio versus the false positive (FP) ratio,* Figure 1 results.[4]

It is clear from this figure that if we wish to detect all patients with

*The true positive (TP) ratio is the conditional probability of an abnormal test result given that the patient has the disease. The false positive (FP) ratio is the conditional probability of an abnormal test result given that the patient does not have the disease.

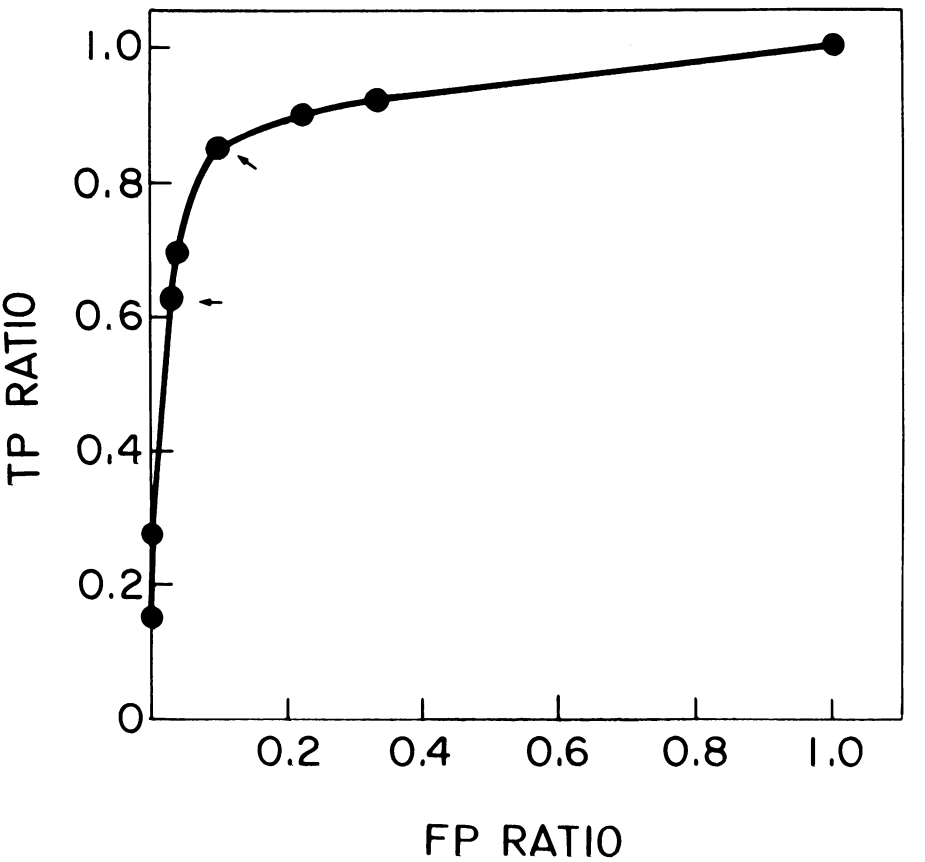

Fig. 1. Receiver operating characteristic (ROC) curve for the renogram (RG). The true-positive (TP) ratio is plotted on the ordinate against the false-positive (FP) ratio on the abscissa.

renovascular disease (TP ratio = 1.0), then we also shall have a high FP ratio. Thus, the certainty with which we can say that a patient has renovascular disease on the basis of an abnormal examination is low. If, on the other hand, we are more strict in our operating position and make the TP ratio low, 0.3 for example, the FP ratio drops to 0 and we can be certain of the diagnosis of renovascular disease in the face of an abnormal examination. A continuum of conditional probabilities is possible between these points.

This investigation studied in detail the results expected from operating at two positions on this curve. The first or more strict operating position has

TABLE I. COMPOSITION OF A REPRESENTATIVE HYPERTENSIVE POPULATION OF 100 PATIENTS

	Patients (No.)
No identifiable cause or "essential hypertension" (RVD−)	90
Renovascular disease (RVD+)	10
Atherosclerotic disease (9% operative mortality; 44% surgical cure)	6.7
Fibromuscular disease (3% operative mortality; 60% surgical cure)	3.3

a TP ratio of 0.63 and an FP ratio of 0.03. This position corresponds to maximizing the expected value of our decision, where the costs of making an incorrect decision are 0 and the values of correct decisions are 1. The second operating position was more lax, that is, the TP ratio was higher—0.83. This position was chosen on the basis of information theory to maximize the informational content of the examination; its use was suggested by Metz in a study in *Radiology*.[5] Hereafter, these two operating positions will be referred to as strict and lax, respectively.

The IVP alone does not allow a continuum of TP and FP diagnoses. Rather, it usually is graded on the basis of one or more abnormalities in the appearance time, calyceal concentrations, or kidney length. For these criteria, the associated TP ratio is 0.78 and the FP ratio is 0.11.[6] These are similar to results from the RG at a lax operating position.

Before the results of these tests are compared in terms of sensitivity and specificity, it is necessary to review the average hypertensive population on which they will be performed. For the purposes of this study it was assumed that of 100 patients with high blood pressure, 90 would have essential hypertension. The remaining 10 patients were assumed to have renovascular disease; of these, 6.7 were assumed to have atherosclerotic disease and 3.3 fibromuscular disease[7] (see Table I). The aim was to locate all patients with renovascular disease and to define angiographically the nature of their disease.

Table II compares the results of the IVP and RG alone and in combination among a representative sample of 100 patients. This table was made by combining the prior probability of disease (0.10) with the conditional probabilities indicated earlier for the RG and IVP. The second column indicates that none of these tests ever finds all 10 patients with renovascular disease. The RG at a lax operating position finds the most, nine, but at

TABLE II. RESULTS OF SCREENING 100 PATIENTS FROM AN AVERAGE HYPERTENSIVE POPULATION

Test	Patients with positive tests (no.)	
	RVD+ (10 patients)	RVD– (90 patients)
Intravenous pyelogram	8	10
Renogram (TP ratio = 0.85)	9	9
Renogram (TP ratio = 0.62)	6	3
Intravenous pyelogram and renogram (TP ratio = 0.62) both abnormal	5	0

RVD+ = patients who have renovascular disease, RVD– = patients who do not have renovascular disease

the expense of including many patients without renovascular disease, also nine. Varying results exist for the RG at a more strict operating position or the IVP at its only operating position. An interesting result occurs when the IVP is coupled with the RG and the latter evaluated at a strict operating position. Here five out of 10 patients with renovascular disease are found, and no patients without this disease are abnormal on both tests.

The next step in our cost-effectiveness analysis was determination of the relative costs of finding patients with renovascular disease by these modalities. For these calculations we have estimated that an RG costs $100, an IVP $83, and renal arteriography $375. When either the IVP or RG is used for screening, it costs approximately $2,000 per patient for the discovery of between 60% and 90% of patients with renovascular disease. When both tests are used and arteriography is performed only on those with both examinations abnormal, the cost rises to more than $4,000 per patient found, and only 50% of patients with renovascular disease are found.

Let us now consider the total hypertensive population in the United States, not only in terms of the cost of finding cases but also in terms of the cost of surgery on patients with renovascular disease. The following assumptions were used for these calculations:

1) The total hypertensive population in the United States numbers 23 million.

2) One third of these individuals have fibromuscular renovascular disease and two thirds have atherosclerotic disease.

3) Deaths result from two sources, angiography and surgery. Angiography is associated with a mortality rate of 0.1% and surgery is associated with a mortality rate of 3% for patients with fibromuscular disease and 9% for patients with atherosclerotic disease.[8-10]

TABLE III. COST-EFFECTIVENESS ANALYSIS FOR THE DIAGNOSTIC WORK-UP AND SURGICAL TREATMENT IN THE TOTAL HYPERTENSIVE POPULATION OF THE UNITED STATES

	Screening method	
	Intravenous pyelogram (true positive ratio = 0.78)	*Intravenous pyelogram and renogram (true positive ratio = 0.62)*
Total cost	$\$12.5 \times 10^9$	$\$9.90 \times 10^9$
Deaths (no.)	130,000	75,000
Surgical cures	827,000	494,000
Cost per surgical cure	$15,100	$20,000
Deaths per 100 surgical cures	16	15

4) Sixty percent of patients with fibromuscular disease and 44% of those with atherosclerotic disease are cured surgically.[7]

Table III summarizes the results of these calculations when either the IVP alone or the RG and IVP in concert are used for detection.[4] The total financial costs are of the order of billions of dollars while the actual cost per patient cured varies from $15,100 to $20,000. For both screening strategies the number of deaths per 100 surgical cures is approximately the same, 15 or 16.

An extension of this cost-effectiveness analysis dealt with a comparison between the results of surgical treatment and of other medical treatment for patients with renovascular disease.[11] Figure 2 gives the strategy in terms of a decision-flow diagram. The first strategy involves screening for renovascular disease and then operating on those patients with either fibromuscular or atherosclerotic disease and treating the remaining patients by medication. The second strategy involves treating all patients with drugs alone regardless of the etiology of their hypertension. The results of these strategies are displayed in Figure 3. In both cases, at the end of the flow diagram is a chance node indicating the patient's state: i.e., he is well, he has suffered a nonfatal morbid event (coronary heart disease, cerebrovascular accident), or he is dead.

This study compared the number of patients in these categories with each strategy in relation to varying initial diastolic blood pressures. Data collected by the Framingham Study on Cardiovascular Disease were used to estimate the probabilities of fatal and nonfatal morbid events and to calculate the outcomes assuming a 16-year follow-up.[12-13] Because outcomes are influenced markedly by the compliance of patients, it was

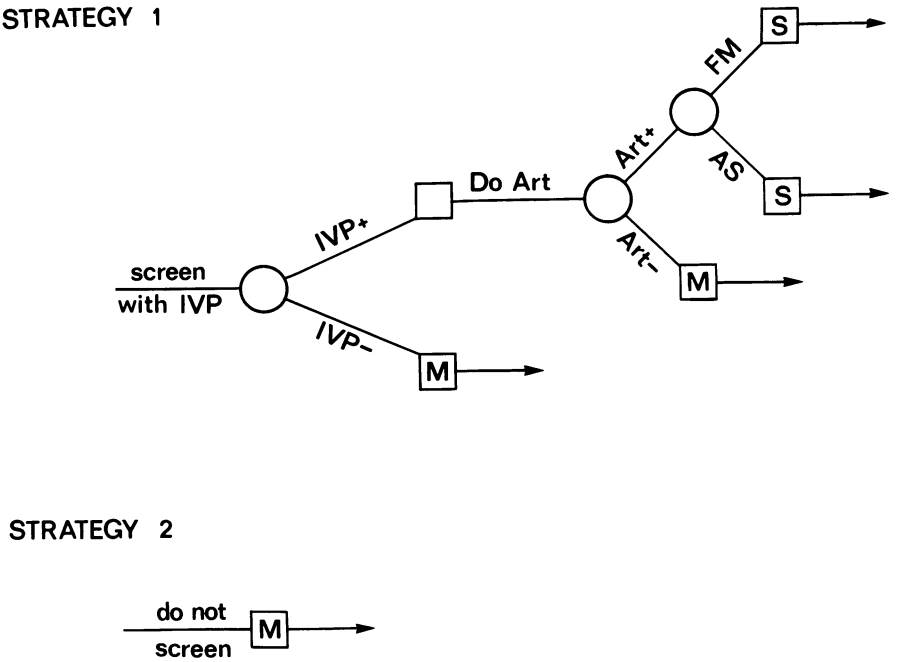

Fig. 2. Decision-flow diagrams for treatment of patients with hypertensive disease. *Strategy 1:* Screening is performed on all patients with hypertension. If the result of the intravenous pyelogram (IVP) is abnormal (IVP+), arteriography (Art) is always performed. When the results of the IVP and arteriogram are normal (IVP- and Art-, respectively), however, medical therapy (M) is followed. When the arteriogram is positive (Art+), surgery (S) is chosen for patients with fibromuscular (FM) and atherosclerotic (AS) disease. The outcomes of the use of surgery and medication are shown in Figure 3. *Strategy 2:* No screening intravenous pyelograms are done and all patients are treated with medication (M), the results of which are shown in Figure 3.

necessary to introduce this variable into the calculations. We studied two states of this variable. The first, 50% compliance, corresponded to the usual clinical situation—25% of patients are cured, 25% are improved, and 50% are lost to follow-up. The second, 84% compliance, is unusually high—84% are cured and 16% are lost to follow-up.[14]

Figure 4 summarizes the results of these calculations by indicating the differences in outcomes between the surgical and medical strategies. Thus, when deaths are enumerated, the medical regimen (upper part of graph) appears better than the surgical one in nearly all instances. Only at high diastolic blood pressures (135 mm. Hg) and low compliances do the surgical results approach the medical ones. When nonfatal morbid events are enumerated, surgery always appears better and when the number of

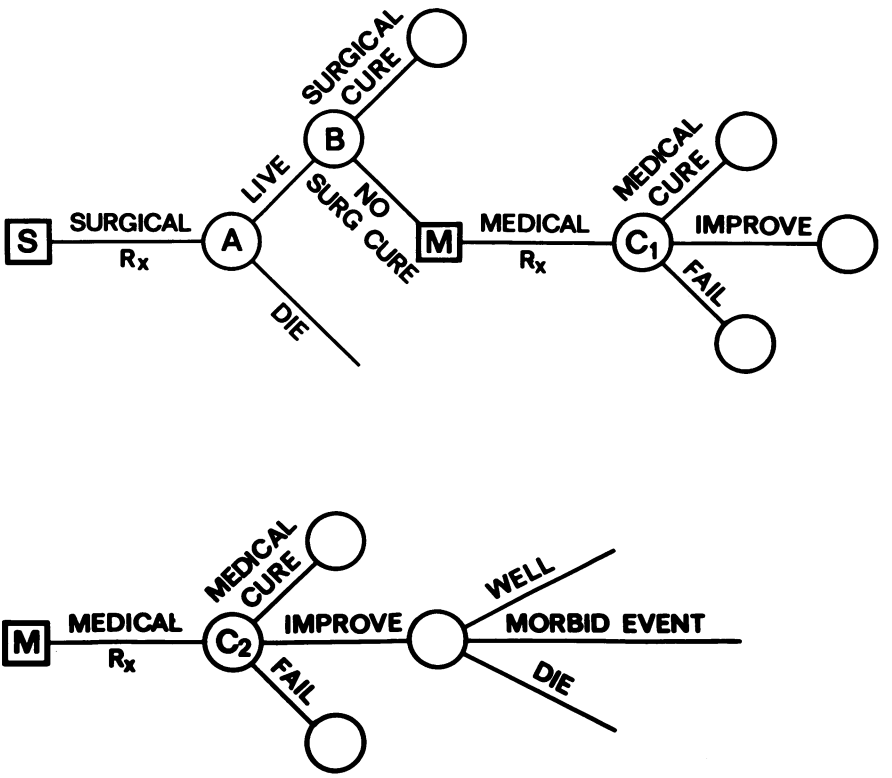

Fig. 3. Outcomes associated with the surgical and medical regimens. The results of surgery on patients with renovascular disease are detailed at chance nodes A and B. Results of primary or supplemental medical therapy are expressed at nodes C_1 and C_2. All of the terminal chance nodes are associated with three possible outcomes: well, morbid event, or death. Reproduced by permission from McNeil, B. J. and Adelstein, S. J.: Measures of clinical efficacy, *New Eng. J. Med. 293*:221-26, 1975.

well patients are considered medical therapy appears better for all levels of diastolic blood pressure at high rates of compliance. At lower compliances and higher blood-pressure levels surgery offers an advantage. Obviously, an index which weights these three categories rather than considering them individually would be best for comparing the results of these therapeutic strategies. Unfortunately, however, no such index is available.

In summary, three conclusions can be drawn from this analysis:

1) The total financial cost of the diagnosis of hypertensive renovascular disease is of the order of billions of dollars when we consider the work-up of the total hypertensive population in the United States. Obviously, this cost will drop if we develop criteria to select only a fraction of this

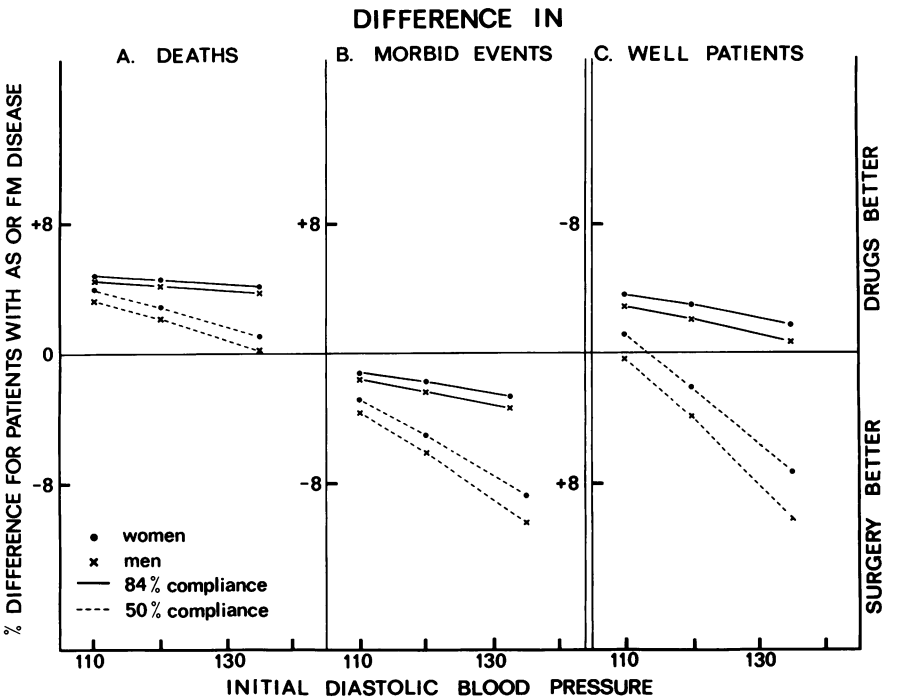

Fig. 4. Difference in the number of deaths (Panel A), nonfatal morbid events (Panel B), and well patients (Panel C) as a function of sex, compliance, and initial diastolic blood pressure. The ordinate represents the percentage difference in the results of surgical and medical therapy in patients with renovascular disease. Note that negative differences in deaths or nonfatal morbid events favor surgical treatment and negative differences in well patients favor medical treatment. AS=atherosclerotic, FM=fibromuscular. Reproduced by permission from NcNeil, B. J. and Adelstein, S. J.: Measures of clinical efficacy. *New Eng. J. Med. 293*:221-26, 1975.

population for examination. The cost of detecting patients with renovascular disease is from $2,000 to $4,000 per patient found (when scintigraphic and radiographic methods are used). The cost of a cure rises nearly tenfold, to $15,000 to $20,000 per patient.

2) For every 100 surgical cures there are 15 to 16 deaths when patients with either fibromuscular or atherosclerotic disease are considered surgical candidates. This figure will drop if only patients with fibromuscular renovascular disease are considered surgical candidates.

3) Our model comparing the results of medical and surgical therapy indicates that the choice between these modalities depends strongly on the compliance of patients as well as on diastolic blood pressure.

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